

DEPARTMENT OF HEALTH & HUMAN SERVICES



Public Health Service

Food and Drug Administration
2094 Gaither Road
Rockville MD 20850

JAN 8 2007

WARNING LETTER

VIA FEDERAL EXPRESS

Charles D. O'Shaughnessy, MD
North Ohio Heart Center
125 E. Broad Street
Elyria, OH 44035

Dear Dr. O'Shaughnessy:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at your clinical site from October 26 through November 9, 2006, by investigators from the FDA Cincinnati District Office. The purpose of this inspection was to determine whether activities and procedures related to your participation in the studies titled [REDACTED]

[REDACTED] (designated herein as the [REDACTED] study), under [REDACTED], sponsored by [REDACTED], and [REDACTED]

[REDACTED] (designated herein as the [REDACTED] study), under [REDACTED], sponsored by [REDACTED], [REDACTED], complied with applicable federal regulations. The coronary stents used for both studies are devices as that term is defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 321(h). This letter also discusses your November 10, 2006, written response to the observations noted at the time of the inspection, and requests that you promptly implement corrective actions.

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval (PMA) applications, and Premarket Notification submissions (510(k)) are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report prepared by the district office revealed several serious violations of Title 21, Code of Federal Regulations (21 CFR.) Part 812 -- Investigational Device Exemptions and Part 50 -- Protection of Human Subjects. At the close of the inspection, the FDA investigators presented a form FDA 483 -- "Inspectional Observations" for your review, and discussed the observations listed on

the form with you. The deviations noted on the FDA 483, your written response, and our subsequent review of the inspection report are discussed below:

1. Failure to ensure an investigation is conducted in accordance with the signed agreement with the sponsor, the investigational plan, applicable FDA regulations, and any conditions of approval imposed by FDA or the IRB [21 CFR 312.100, 21 CFR 312.110(b)].

Regarding the [redacted] study, you failed to adhere to the above-stated regulations. Examples of this failure include but are not limited to the following:

- a.) At least 8 of the 47 subjects enrolled in the study failed to meet eligibility criteria. Specifically:
- i. Subject [redacted] had a non-study [redacted] less than 24 hours prior to the study procedure, which was prohibited by the study protocol.
 - ii. Subjects [redacted] and [redacted] each received a non-study, [redacted] stent in a [redacted] prior to the study procedure, which was a clinical exclusion criterion.
 - iii. Subject [redacted] was being treated with [redacted] on admission to the hospital and after the study procedure, which was prohibited by the study protocol.
 - iv. Subject [redacted] had a baseline [redacted] which showed the [redacted] [redacted]. The [redacted] was [redacted] for the study, while the protocol requires the [redacted].
 - v. Subjects [redacted] and [redacted] had pre-procedure [redacted], which was a clinical exclusion criterion.
- b.) The study protocol states "[redacted]
[redacted]
[redacted]" At least 13 of the 47 subjects enrolled in the study (Subjects [redacted] and [redacted]) [redacted]
[redacted]
- c.) The protocol specified that [redacted]
[redacted], and provided a guide for [redacted]
[redacted]. The protocol also stated "[redacted]
[redacted]
[redacted]"
[redacted]. Specifically:

to perform study tasks delegated to them. You may delegate study tasks to other qualified personnel, but you may not delegate your responsibility to ensure that all study tasks are correctly performed.

As a Clinical Investigator, you are also required to follow the study protocol exactly as it is written, unless the protocol is amended by the study sponsor or the study sponsor gives prior approval for a protocol deviation. The [] study protocol states "this protocol is to be followed exactly, and will only be altered by written amendments." Additionally, you and your co-investigators also signed a Clinical Study Agreement in which you agreed to take responsibility for conducting the study according to the protocol and to supervise all testing of the study device.

2. Failure to maintain accurate, complete, and current records of each subject's case history and exposure to the device [21 CFR 812.140(a)(3)].

Regarding the [] study, you failed to adhere to the above-stated regulations. Examples of this failure include but are not limited to the following:

- a.) The baseline percentage of study vessel blockage as recorded in the study records was inconsistent for at least 6 of the 47 subjects enrolled into the study. For example:
 - i. Subject []: the [] at baseline and the discharge summary record [] for the [], while the case report form (CRF) worksheet and procedure summary record it as [].
 - ii. Subject []: the [] at baseline and the written procedure note records [] for the [], while the CRF worksheet and procedure summary record it as [].
 - iii. Subject []: the CRF worksheet records [] for the [] while the procedure summary records it as [].
 - iv. Subject []: the [] at baseline records [] for the [], while the CRF worksheet and procedure summary record it as [].
 - v. Subject []: the [] at baseline records [] for the [] and the remainder of the [] as [], while the CRF worksheet and procedure summary record the [] as the [] with [].
 - vi. Subject []: the [] at baseline records [] for the [] while the CRF worksheet and procedure summary record it as 80%.
- b.) Other inconsistencies in the study records include:
 - i. Subject []: your response letter notes that [] totaling [] were used for the subject "to []". However, there is no mention of [] in the study records.
 - ii. Subject []: the CRF worksheet records the [] as the [] which the baseline [] reports as []. The procedure summary records the [] as the [] which the baseline [] reports as normal.

Regarding the [] study, you failed to adhere to the above-stated regulations. An example of this failure includes but is not limited to the following:

- c.) The study records for Subject [] variously record the [] as a []
[] (procedure flow sheet), a [] (procedure report), or a []
[] (CRF worksheet).

The violations described above are not intended to be an all inclusive list of problems that may exist with your clinical study. It is your responsibility as a clinical investigator to ensure compliance with the Act and applicable regulations.

Within fifteen (15) working days of receiving this letter, please provide written documentation of the actions you have taken or will take to correct these violations and prevent the recurrence of similar violations in current or future studies for which you are the clinical investigator. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. In addition, FDA could initiate disqualification proceedings against you in accordance with 21 CFR. 812.119.

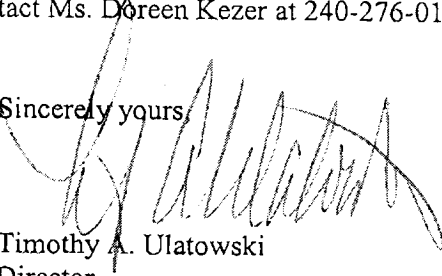
You will find information to assist you in understanding your responsibilities and planning your corrective actions in the FDA Information Sheets Guidance for Institutional Review Boards and Clinical Investigators, which can be found at <http://www.fda.gov/oc/ohrt/irbs/>. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Please send your response to:

Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance, Division of Bioresearch Monitoring, HFZ-311
9200 Corporate Blvd., Rockville, Maryland 20850
Attention: Ms. Doreen Kezer, Chief, Special Investigations Branch.

A copy of this letter has been sent to the FDA Cincinnati District Office, 6751 Steger Drive, Cincinnati, OH 45237. Please send a copy of your response to that office.

If you have any questions, please contact Ms. Doreen Kezer at 240-276-0125 or at Doreen.Kezer@fda.hhs.gov.

Sincerely yours,


Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and Radiological Health

IRB/Purged Copy to:

EMH Regional Medical Center IRB
630 East River St.
Elyria, OH 44035

Sponsor/Purged Copy to:

and